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(54) Title: 50 HUMAN SECRETED PROTEINS

(57) Abstract: The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

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***What Is Claimed Is:***

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group

5 consisting of:

(a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

10 (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

15 (d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(e) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X,  
20 having biological activity;

(f) a polynucleotide which is a variant of SEQ ID NO:X;

(g) a polynucleotide which is an allelic variant of SEQ ID NO:X;

(h) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;

(i) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(h), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.

5

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a secreted protein.

10

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.

15

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.

20

5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

25

6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.

5 8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.

9. A recombinant host cell produced by the method of claim 8.

10 10. The recombinant host cell of claim 9 comprising vector sequences.

11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

- 15 (a) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
- (b) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z, having biological activity;
- (c) a polypeptide domain of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
- 20 (d) a polypeptide epitope of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
- (e) a secreted form of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
- (f) a full length protein of SEQ ID NO:Y or the encoded sequence included in
- 25 ATCC Deposit No:Z;
- (g) a variant of SEQ ID NO:Y;

- (h) an allelic variant of SEQ ID NO:Y; or
- (i) a species homologue of the SEQ ID NO:Y.

12. The isolated polypeptide of claim 11, wherein the secreted form or the full length protein comprises sequential amino acid deletions from either the C-

5 terminus or the N-terminus.

13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.

10 14. A recombinant host cell that expresses the isolated polypeptide of claim 11.

15. A method of making an isolated polypeptide comprising:

- (a) culturing the recombinant host cell of claim 14 under conditions such that
- 15 said polypeptide is expressed; and
- (b) recovering said polypeptide.

16. The polypeptide produced by claim 15.

20 17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

25 18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

5

19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and

10 (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:

15 (a) contacting the polypeptide of claim 11 with a binding partner; and

(b) determining whether the binding partner effects an activity of the polypeptide.

21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.

20

22. A method of identifying an activity in a biological assay, wherein the method comprises:

(a) expressing SEQ ID NO:X in a cell;

(b) isolating the supernatant;

25 (c) detecting an activity in a biological assay; and

(d) identifying the protein in the supernatant having the activity.

23. The product produced by the method of claim 20.

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<223> Xaa equals any of the twenty naturally occurring L-amino acids

<400> 84

Phe Leu Ile Ser Leu Cys Ile Leu Ile Pro Phe Leu Ile Leu Ser Pro  
1 5 10 15

Xaa

<210> 85

<211> 233

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (233)

<223> Xaa equals any of the twenty naturally occurring L-amino acids

<400> 85

Met Pro Ser Leu Trp Asp Arg Phe Ser Ser Ser Ser Thr Ser Ser Ser  
1 5 10 15

Pro Ser Ser Leu Pro Arg Thr Pro Thr Pro Asp Arg Pro Pro Arg Ser  
20 25 30

Ala Trp Gly Ser Ala Thr Arg Glu Glu Gly Phe Asp Arg Ser Thr Ser  
35 40 45

Leu Glu Ser Ser Asp Cys Glu Ser Leu Asp Ser Ser Asn Ser Gly Phe  
50 55 60

Gly Pro Glu Glu Asp Thr Ala Tyr Leu Asp Gly Val Ser Leu Pro Asp  
65 70 75 80

Phe Glu Leu Leu Ser Asp Pro Glu Asp Glu His Leu Cys Ala Asn Leu  
85 90 95

Met Gln Leu Leu Gln Glu Ser Leu Ala Gln Ala Arg Leu Gly Ser Arg  
100 105 110

Arg Pro Ala Arg Leu Leu Met Pro Ser Gln Leu Val Ser Gln Val Gly  
115 120 125

Lys Glu Leu Leu Arg Leu Ala Tyr Ser Glu Pro Cys Gly Leu Arg Gly  
130 135 140

Ala Leu Leu Asp Val Cys Val Glu Gln Gly Lys Ser Cys His Ser Val  
145 150 155 160

Gly Gln Leu Ala Leu Asp Pro Ser Leu Val Pro Thr Phe Gln Leu Thr  
165 170 175

Leu Val Leu Arg Leu Asp Ser Arg Leu Trp Pro Lys Ile Gln Gly Leu  
180 185 190

Phe Ser Ser Ala Asn Ser Pro Phe Leu Pro Gly Phe Ser Gln Ser Leu

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195

200

205

Thr Leu Ser Thr Gly Phe Arg Val Ile Lys Lys Lys Leu Tyr Ser Ser  
 210 215 220

Glu Gln Leu Leu Ile Glu Glu Cys Xaa  
 225 230

&lt;210&gt; 86

&lt;211&gt; 131

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (131)

&lt;223&gt; Xaa equals any of the twenty naturally occurring L-amino acids

&lt;400&gt; 86

Met Tyr Gln Thr Pro Met Glu Val Ala Val Tyr Gln Leu His Asn Phe  
 1 5 10 15

Ser Ile Ser Phe Phe Ser Ser Leu Leu Gly Gly Asp Val Val Ser Val  
 20 25 30

Lys Leu Asp Asn Ser Ala Ser Gly Ala Ser Val Val Ala Ile Asp Asn  
 35 40 45

Lys Ile Glu Gln Ala Met Asp Leu Val Lys Asn His Leu Met Tyr Ala  
 50 55 60

Val Arg Glu Glu Val Glu Ile Leu Lys Glu Gln Ile Arg Glu Leu Val  
 65 70 75 80

Glu Lys Asn Ser Gln Leu Glu Arg Glu Asn Thr Leu Leu Lys Thr Leu  
 85 90 95

Ala Ser Pro Glu Gln Leu Glu Lys Phe Gln Ser Cys Leu Ser Pro Glu  
 100 105 110

Glu Pro Ala Pro Glu Ser Pro Gln Val Pro Glu Ala Pro Gly Gly Ser  
 115 120 125

Ala Val Xaa  
 130

&lt;210&gt; 87

&lt;211&gt; 37

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (37)

&lt;223&gt; Xaa equals any of the twenty naturally occurring L-amino acids

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